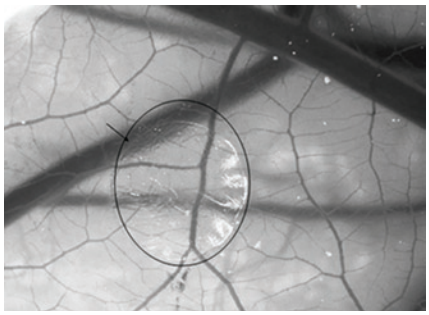
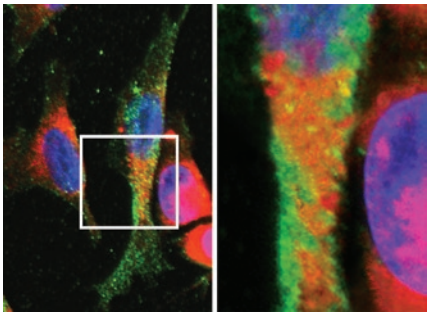
Understanding Psoriasis Treatment



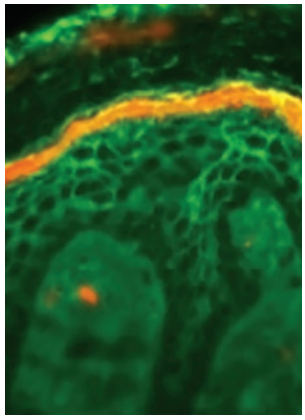
The fumaric acid ester dimethylfumarate (DMF) and its metabolites have been used for some 50 years to treat psoriasis, the features of which include angiogenesis-related pathology. García-Caballero and colleagues found that DMF inhibits the differentiation, proliferation, and migration of endothelial cells *in vitro* in a dose-dependent fashion. Chick chorioallantoic membrane and zebrafish embryo neovascularization assays revealed that DMF inhibited *in vivo* angiogenesis. This function of DMF may explain the previously reported antipsoriatic, antitumoral, and antimetastatic activities of this compound. Furthermore, the results suggest that DMF may be a useful therapy for angiogenesis-related malignancies. ***See page 1347***

Enlightening Therapy



The vitiligo-inducing compound monobenzone induces a robust antimelanoma immunity involving a $CD8^+$ T-cell response. In studies to address the mechanism of this action, van den Boorn and colleagues demonstrated that monobenzone inactivated the tyrosinase pigment-synthesis enzyme. In addition, monobenzone exposure generated quinine-haptens, melanosome autophagy, and secretion of melanocyte antigen–containing exosomes in response to induced reactive oxygen species. Moreover, this monobenzone treatment activated dendritic cells and resulted in a strong T-cell immunity against the melanoma cells. This potent immune response against pigmented cells offers an opportunity in the field of cancer immunotherapy. ***See page 1240***

Barrier Protein Alterations



Tumor necrosis factor (TNF)-α overexpression and epidermal barrier deficiency have both been implicated in the pathogenesis of psoriasis. Kim and colleagues observed that expression of the epidermal barrier proteins filaggrin and loricrin was decreased in lesional and nonlesional skin of psoriasis patients as well as in primary human keratinocytes treated with TNF-α and that these alterations occurred via a c-Jun N-terminal kinase–dependent pathway. Importantly, patients treated with the TNF-α antagonist etanercept exhibited increased expression of filaggrin and loricrin in concert with clinical disease improvement. These data indicate that barrier protein deficiency in psoriasis patients may be acquired through TNF-α-mediated downregulation. ***See page 1272***

Flavonoids in the Diet

Fisetin, a naturally occurring flavonol with neuroprotective and anticancer properties, was shown to decrease the viability of human melanoma cells via G1 cell cycle arrest. These antiproliferative effects resulted from interference with key elements of the Wnt/β-catenin signaling pathway, which has previously been shown to be activated constitutively in malignant cancers, including melanoma. Inhibition of growth of xenografted melanomas and decreased expression of the Wnt downstream target microphthalmia-associated transcription factor were observed in mice treated with fisetin. These findings provide strong evidence that fisetin may be used as a chemopreventive or therapeutic compound against melanoma. ***See page 1291***

Differential Degradation

Modulation of skin pigmentation occurs via interruption of melanin biosynthesis or inhibition of melanosome transfer from melanocytes to keratinocytes. The mechanism of melanosome processing after transfer via melanosomal degradation is a topic of interest. Ebanks and colleagues developed a novel system involving fluorescent labeling of melanosomes and subsequent analysis using transmission electron microscopy, indirect immunofluorescence with confocal microscopy, and flow cytometry. As compared with keratinocytes from dark skin, keratinocytes from light skin consistently exhibited a higher rate of melanosomal loss, suggesting that differential pigment degradation occurs in different skin types. ***See page 1226***

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